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Witches, Pubertal Development, and "Minimal Risk"

[Editorial]

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Outline

A FEW YEARS AGO, we rented the videotape of Roald Dahl's book *The Witches*. My kids generally like Dahl, especially *Charlie and the Chocolate Factory*, and we thought that *The Witches* might be a fun movie. It was a big mistake. The movie starts out in the home of a happy, loving family. It evokes Disneylike comfort and charm. The attentive parents are going out to dinner, and their son is staying with his grandmother. He is scared because his parents are leaving. They assure him that they will be home soon and kiss him good night. Then things start to go bad.

His grandmother reads him a bedtime story about frightening witches. His parents are killed in a gruesome car wreck. In this movie, many kindly adults who seem to want to help children are really witches in disguise who want to turn children into mice. One group of witches surreptitiously meets as a convention of the Society for the Prevention of Cruelty to Children. When they get into the convention hall, they lock the doors and peel off their human-appearing rubber masks to reveal horrendous witch faces underneath. At this point our daughter Tess, who was then 5 years old, ran screaming from the living room and for the next 6 months had trouble falling asleep in her own bed.

Clearly, we had underestimated the psychological harm that might ensue from watching this frightening and complex movie. Thus, we were somewhat surprised and apprehensive when our youngest daughter, Emma, turned 7 years old, read the book, and said that she wanted to see the movie. We tried to stall, but she was insistent. We finally gave in and, with numerous warnings about how stressful it was going to be, put the tape in the videocassette recorder. Emma loved it. She cried when the parents died, giggled when the witches peeled off their masks, and loved the scenes where kids were turned into mice. She watched it again and again. She is a big Dahl fan and even bought his cookbook, *Roald's Revolting Recipes.* One night Emma treated us all to a dinner of snozzcumbers.

The dilemma we faced in deciding whether to allow our children to watch a movie was, in some respects, similar to that faced by institutional review boards (IRBs) evaluating the psychological effects of various research projects involving children. Would or should an IRB have approved a project if it included watching Roald Dahl movies?

Research involving children is always morally problematic. Such research is important to understand children's unique physiologic and pathologic characteristics. This knowledge allows better medical treatment of

pediatric problems. However, children often cannot fully understand the risks and benefits of research, so they cannot give fully informed consent. Instead, children are asked to give their assent to participation, and parents are asked for their permission to allow their children to participate. In the United States and Canada, a widespread consensus seems to have developed around the issue of pediatric research ethics. According to this consensus, research projects should be reviewed and approved by impartial ethics committees before they are conducted. These committees must decide whether the studies involve no risk, minimal risk, or a minor increment above minimal risk.

According to the IRB guidebook published by the United States Department of Health and Human Services, "[T]o safeguard their interests and to protect them from harm, special ethical and regulatory considerations are in place for reviewing research involving children" [1] (Title 45 CFR Part 46, subpart D, addresses protections in place for children). Minimal risk is defined as follows:

A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

This standard is operationalized through the process of review by IRBs. Members must weigh the probable risks and discomforts of a research study and decide whether they are excessive. If so, they will not approve the protocol. However, because there are no precise measures of risk or discomfort, the IRB review process is often idiosyncratic. Different IRBs may make different decisions about the same protocol.

When McCarthy et al [2] proposed a study that involved 4 overnight hospital admissions, examination of pubertal development, and intravenous insertion for obtaining blood, most IRBs would have responded in 1 of 2 extreme ways. They might have simply decided that the study involved minimal risk and approved it, or they could have decided that it posed greater than minimal risk and rejected it. Instead, the members of the IRB at the University of Iowa (Iowa City) had an interesting, innovative, and important response. They requested that the researchers systematically and quantitatively assess the risks of the study for each participant. In this particular study, they used pediatric psychologists to identify appropriate participants and to follow up with these children to determine aftereffects.

The results of the quantification of risk in the study by McCarthy and colleagues are interesting and informative. For example, the role of anxiety was underscored. Screening children for anxiety and other aspects of emotional functioning may help predict which subjects will be adversely affected by participation in invasive nontherapeutic research. Another important finding was that responses to the questionnaires as well as the level of understanding and anxiety about participating varied for different children, between parents and children, and in the pretesting and posttesting of participants. The highest levels of anxiety were not associated with the interventions of most concern to the IRB. The IRB was most concerned about the overnight hospitalization. Parental perceptions were that intravenous insertion would cause the most distress. For the children, the assessment of pubertal development was "the most concerning aspect" of the study.

Follow-up with research participants as well as independent assessments of parents and children may be a key method for more accurately assessing potential risks. Data accrued across studies can be used for evaluating the minimal risk of future studies within a reasonably similar context.

The process of assessing risk raises some concerns. First, is the process of undergoing psychological screening yet another protocol that requires IRB approval, or are tests of cognitive and emotional functioning routine? Going through a psychological screening is anxiety provoking for some children.

Second, we might ask what these standard psychological tests really measure. Whereas measures such as those used by the researchers in the article by McCarthy and colleagues have high reliability and construct validity, the ecological validity of these measures is less robust. This is less of a concern for cognitive screening than for anxiety and depression screening. Self-report measures may not predict how the child will react in a real-life context or allow us to determine if a child has been psychologically harmed. Screening for emotional functioning and/or personality variables may provide important and reliable ways to assess potential psychological harm but may not completely capture the risks posed to child participants.

Third, such testing has implications for follow-up. In any project, the researchers have an obligation to provide care for subjects who experience harm as a consequence of their participation. In this case, the use of psychological screening tests might reveal adverse psychological consequences. For example, a child may have nightmares about the invasive research procedure. Increased knowledge about such sequelae creates increased moral obligations.

Finally, it is unclear how researchers should interpret such data as they begin the process of obtaining informed consent. In the study by McCarthy and colleagues, none of the children reported concerns about participating before it was conducted, but 45% later reported that they had been concerned prior to participation. Such discordant answers raise concerns about the motivations of children and their parents. Were they deliberately lying to researchers because they wanted to participate? If so, was it because they wanted the money? Such results highlight the need to be attentive to the possibility of coercion.

Like all good research, the authors' study raises more questions than it answers. Quantifying and elaborating specific psychological risk factors among particular children prior to their participation in invasive nontherapeutic research is a promising path for systematically addressing the complexities of evaluating minimal risk. This is a more stringent and consistent standard for assessing minimal risk and accounting for individual personality and emotional factors than is generally used. It may lead to a more conservative reading of the Department of Health and Human Services guidelines. For example, these guidelines state, "Procedures that usually present no more than minimal risk to a healthy child include: urinalyses, obtaining small blood samples, EEGs [electroencephalograms], allergy scratch tests, minor changes in diet or daily routine, and/or the use of standard psychological or educational tests." If we think of the term *healthy* in this statement as referring to psychological as well as physical health, more children may be ineligible for participation in research.

Reliable, valid, and flexible methods for evaluating minimal risk in children, such as those used in the study by McCarthy and colleagues, will help delineate the risks of participating in invasive nontherapeutic research. Children's psychological responses to research protocols are likely to be as individual and idiosyncratic as their responses to movies or to other experiences in life. It may turn out that the minimal risk standard is best applied not to a particular protocol but to each child participant in each study. Although this would be more labor intensive, it might help us understand the moral and emotional issues surrounding research and ultimately better protect the children who are subjects in scientific studies.

References

1. Penslar RL. Protecting human research subjects: Institutional Review Board guidebook. US Department of Health and Human Services Office for Human Research Protections Web site. Available at: http://ohrp.osophs.dhhs.gov/irb/irb_guidebook.htm . Accessed September 4, 2001. [Context Link]

2. McCarthy AM, Richman LC, Hoffman RP, Rubenstein L. Psychological screening of children for participation in nontherapeutic invasive research. Arch Pediatr Adolesc Med. 2001;155:1197-1203. **Ovid Full Text** **Bibliographic Links** [Context Link]

Anxiety; Child Psychology; Ethics, Medical; Informed Consent; Patient Selection; Research; Risk Assessment

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